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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,609	08/17/2000	Yoshinari Kumagai	BEAR-004	6929

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/642,609	KUMAGAI ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *24 June 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *12-16 and 20-22*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

ROBERT A. WAX
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: The rejection under 35 U.S.C. 103(a) over the prior art of record is maintained. Applicant's arguments that the primary reference of Reylonlds teaches compounds which "significantly increase the absorption of calcium phosphate and iron in the gut." (col. 8, lines 29-31). When more of the phosphate in the food in the patient's gut is absorbed, the phosphate levels in the patient's blood go up. Thus, an increase in absorption of phosphate from the gut would be expected to increase serum phosphate levels, not to decrease serum phosphate levels, as presently claimed is unpersuasive. Contrary to Applicant's arguments, the prior art of Reynolds renders the claim obvious because it teaches a composition comprising a phosphopeptide having 5-30 amino acids, wherein the composition is in a form of pharmaceutical composition and administered orally to a mammal in a therapeutically effective amount (See e.g., col. 1, lines 10 to col. 2, lines 8 and col. 3, lines 9-14). The reference of Reynolds on col. 2, lines 50-68 further teaches that the composition preferably comprises a peptide which is present as 0.01 to 10% by weight which is a unit of 1 to 1000, and as such is equivalent to a composition comprising 1 to 1,000 mg of the peptide compound as claimed in claim 13 (i.e., since mg reflects weight unit). Also, the reference discloses that the peptidic compound exhibits a reduction in hydroxyapatite dissolution rate of at least 15% which meets the limitation of reduction serum phosphate levels 5% or more of claim 15 because on col. 6, lines 59-61, the reference states that the reduction in hydroxyapatite dissolution was related to phosphoserine content and spacing within a peptide. This is a clear indication of decreasing of phosphate levels.

The references of Reynolds differ from claims 12-16 and 20-22 in not teaching a method of treating hyperphosphatemia (an excess amount of phosphate in the blood) by administering orally the peptidic compound claimed. However, the primary reference of Reynolds on col. 8, lines 27-34 states that the ability of these peptides to sequester calcium phosphate can be utilized in the treatment of various rarefying bone diseases. These peptides can significantly increase the absorption of calcium, phosphate and iron in the gut. Hence, pharmaceutical vehicles (e.g., enteric capsules) or foods containing calcium phosphate T1 and ferrous phosphate T1 can be used for the treatment of osteoporosis/osteomalacia and anemia. Again, contrary to Applicant's arguments this is an indication that phosphate levels decrease. Further, the secondary reference of Monier-Faugere et al., teaches the association of diseases of bone and bone mineral metabolism. For example, on page 1409, the reference teaches the relationship and/or coexistence of calcium, parathyroid hormone (PTH) and phosphate in renal osteodystrophy, which encompasses a wide variety of derangements in mineral and bone metabolism. Furthermore, on page 1410, the reference discloses the associations and mechanisms of how hyperphosphatemia result in advanced renal failure in which the increased serum phosphorus levels and PTH further decreases serum calcium through physicochemical binding affecting the histological pattern of renal osteodystrophy resulting in a profound decrease in bone turnover, i.e., low number of active remodeling sites resulting in bone resorption and suppressed bone formation.

Moreover, the primary reference of Reynolds suggests the treatment of various rarefying bone diseases such as osteoporosis/osteomalacia (i.e., any diseases/conditions associated with increase of phosphate). Thus, in view of this and in view of the secondary reference and in view of the claim language "comprising", one of ordinary skill in the art would understand that the phrase "treatment of various rarefying bone diseases" would include treatment of hyperphosphatemia. Therefore, given the combined teachings of the prior art, one of ordinary skill in the art would be motivated to administer orally the peptidic compound of the primary reference for the intended purpose of treating conditions associated with elevated phosphate levels (i.e., hyperphosphatemia).

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at the time the invention was made to employ a method of treating hyperphosphatemia by administering orally to an individual a therapeutically effective amount of a composition comprising a peptidic compound characterized by a) oral bioavailability, b) 4-30 amino acid residues, and c) having at least one amino acid residue which is phosphorylated or which is phosphorylatable in vivo or in vitro. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including Ex parte Harris, 748 O.G. 586; In re Rosselete, 146 USPQ 183; In re Burgess, 149 USPQ 355 and as exemplified by In re Betz, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them". Therefore, the rejection of claims 12-16 and 20-22 under 35 U.S.C. 103(a) over the prior art of record is maintained for the same reasons discussed in the previous Office action.